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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,795	07/09/2003	Andrew J. Dannenberg	CRF D-2756 NB	8535

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EXAMINER	
ROBERTS, LEZAH	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,795	DANNENBERG ET AL.	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

All rejections have been withdrawn unless stated below.

Claim Rejections - 35 USC § 112 – Written Description/New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite a screening method "for the likelihood of success in treating those at risk or having cancer, Alzheimer's disease or atherosclerosis. Although the Applicant points out support for this claim on page 11 of the specification, there appears to be no support found. The success measurement for each of the diseases now in claim 6 is not disclosed as filed.

Claim Rejections - 35 USC § 112 – Enablement

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are not enabled because all of the screening test are not related to all of the disclosed diseases.

The claims have been analyzed by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the nature of the invention,
2) the breadth of the claims,
3) the relative skill of those in the art,
4) the state of the prior art,
5) the predictability of the art,
6) the amount of direction or guidance provided,
7) the presence or absence of working examples, and
8) the quantity of experimentation necessary.

The nature of the invention. The invention discloses a method of screening a selective COX-2 inhibitor for the likelihood of success in treating a patient having or at risk for cancer, Alzheimer's disease or atherosclerosis, comprising testing of at least two functions recited in a-g.

The State of the Prior Art/The Predictability or Lack Thereof in the Art. It is unpredictable whether a drug can be used to treat a patient having cancer, Alzheimer's disease or atherosclerosis. In the case of cancer, it cannot be predicted if a drug will be successful in treating one type of cancer and this unpredictability increases when trying to treat a broad spectrum of cancers. Although many of the tests are functions related to

cancers, these functions are not related to all cancers. Furthermore, even testing functions that are related to particular cancers can be misleading because a controlled environment *in vitro* cannot predict what will happen *in vivo*. The unpredictable nature of cancer assays has long been recognized. See, *e.g.*, Gura (*Science*, vol. 278, pp. 1041-1042 (1997)), which provides an overview of the problems involved with sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile. Since formal screening began in 1955 many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (second paragraph of the article). As noted therein, the "fundamental problem in drug discovery for cancer is that the model systems are not predictive at all." The reasons are many, including basic differences between human patients on the one hand, and animal and cell culture models on the other (third paragraph of the article).

An efficient means of predicting activity with *in vivo* models remains desirable for compounds with anti-proliferative activity *in vitro* to this day. See the abstract of Johnson et al., *British Journal of Cancer*, vol. 84(10), pp. 1424-1431 (2001). As noted at the bottom of page 1424, the current "drug screening and development scheme remains an empirical one." See also the first paragraph of the "Discussion" section at page 1430 wherein the authors state that "analysis of xenograft versus clinical results illustrates that a histology to histology comparison of these models to activity in the clinic cannot be reliably discerned for these 'empirically' selected compounds acting against non-molecularly characterized tumours."

In the case of Alzheimer's disease (AD), the screening test recited in the claims have little or no relation to AD. AD is difficult to diagnose. According to the National Institute of Aging, the only way to diagnose AD is to find out whether there are plaques and tangles in brain tissue. To look at brain tissue, however, doctors must usually wait until they do an autopsy. Therefore, doctors can only make a diagnosis of "possible" or "probable" AD while the person is still alive. Taking this into account, it would be hard to predict the likelihood of success in treating AD if it cannot be accurately diagnosed that a patient has AD. AD symptoms can vary. The specific problems, along with the rate and severity of decline can vary considerably in different individuals. Indeed most persons with AD can function at a reasonable level and remain at home far into the course of the disorder (MedicineNet.com). Taking this into account, it would be difficult to determine treatment success because there is no clear define way to measure the progression of the disease. According to Firuzi (Ann Neurol (2006) 59:219-228), data obtained from animal models used to study AD, have not been conclusive. The neuropathological hallmarks of AD include deposits of amyloid B (AB) fibrils in senile plaques. AB was measured when COX-2 selective inhibitors were proposed as possible treatment options for AD. When the inhibitors were tested, AB levels did not decrease as predicted (see article on the reasons the inhibitors were predicted to treat AD, page 222, col. 1, paragraph 5). Therefore it may be concluded that one cannot predict whether a drug may be used to treat AD, particularly form screening methods that Applicant has not disclosed the relationship of the methods to AD.

In the case atherosclerosis, Fries (Gastroenterology (2006) 130:55-64) discloses

COX-2 selective inhibitors pose a cardiovascular risk by potentially increasing the likelihood of thrombosis, hypertension and atherogenesis. Celecoxib was one of the drugs that increased the incidence of myocardial infarction and stroke in randomized controlled trials. This inhibitor was disclosed by the Applicant as meeting the criteria for each of the screening methods a-f. Taking the art into account the screening methods disclosed cannot predict the likelihood of success of an inhibitor for the treatment of atherosclerosis.

The Amount of Direction or Guidance Present. The specification does not clearly disclose what would constitute the likelihood of success. It gives no value to of what success is. The specification does disclose prophetic examples but this is not substantial in supporting the claims.

The Presence or Absence of Working Examples. The examples disclosed in the specification are prophetic examples and cannot be relied on as evidence or results utilizing the disclosed invention.

The Breadth of the claims. The claims are broad because they read on three different diseases that have very little if anything to do with one another. The claims are also broad insofar as they do not convey what determines the likelihood of success.

The Quantity of Experimentation Needed. The Applicant's would need to do experiments that show some type of comparison between drugs that meet the criteria of the claims. For instance in the case of cancer, a comparison between a drug that meets all the criteria and one that meets maybe have of the criteria would have to be utilized to determine their effects on one of the diseases. It would have to be shown that the one

that meets all the criteria is more effective than the one that meets half. Experiments would also have to be done to measure the effect of the drug on AD patients such as finding away to measure the plaque and tangles in the brain tissue of a patient and determining any change.

Claims 1-2 are cancelled.

Claims 6-11 are rejected.

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Ardin H. Marschel
Supervisory Patent Examiner
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Ardin H. Marschel 6/12/06

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER